

Evaluation of Stomach Involvement of Non-Hodgkin's Lymphoma: Single Center Experience

Mehmet Şevki Uyanık, Gülsüm Emel Pamuk, Elif Gülsüm Ümit, Muhammet Maden, Ahmet Muzaffer Demir*

*Trakya University, Department of Hematology

Abstract

Introduction: Gastrointestinal tract is the most common site of involvement in non-Hodgkin's lymphomas. Appropriate treatment regimens were not defined because of rare involvement. In the present study we aimed to evaluate treatment response of non-Hodgkin's lymphoma patients with stomach involvement.

Methodology: 26 patients with stomach involvement were retrospectively analyzed between 01/01/1998 and 01/06/2014. Descriptive statistic was performed to analyze data.

Methods: 20 of the patients (76.9%) were composed of primary stomach non-Hodgkin lymphoma, 6 of the patients (23.1%) were composed of patients secondary involvement of the advanced stage disease. All of the patients were subtypes of B cell lymphoma. 3 of the patients (11.5%) was indolent, 22 of the patients (84.6%) was aggressive, and 1 of them (3.8%) was very aggressive. Diffuse large B cell lymphoma was 72.9%; Maltoma was 8.7%, and Mantle cell lymphoma was %3.8. Complete response was achieved at 10 patients, partial response was achieved in 1 patient, and 7 patients were failed to response the treatment. Treatment response and overall survival of low grade and high grade patients, both according to Ann-Arbor and Lugano classification systems were similar. Patients with elevated sedimentation rate had significant lower survival than patients with normal sedimentation rate ($p=0.027$).

Discussion: Together with the data from recent studies, aggressive treatment approach without organ preservation should not be performed on patients without higher inflammatory response and early stage presentation. Sedimentation rate might help to clinicians for the treatment of choice.

Key Words: Non-Hodgkin's lymphoma, stomach involvement, treatment response.

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Introduction

Extra-nodal lymphoma is the term used to define involvement of tissues other than lymph nodes and spleen (1). Extra-nodal non-Hodgkin's lymphoma (NHL) constitutes 25-50% of all lymphomas (2). Extra-nodal disease is usually a part of the systemic advanced stage disease. Incidence of extra-nodal involvement is 0.8-1.5/100.000 annually (3). Median age is 60-70, and male/female ratio is 2/1 (3, 4). Median age at administration is 50 in Turkish population, with a male predominance (5). Gastrointestinal tract is the most common extra-nodal involvement site in NHL. Gastrointestinal system involvement constitutes 30-40% of all extra-nodal sites (6). Stomach is the most common involved organ in gastrointestinal system. Stomach involvement composes 61% of extra-nodal disease (7). Other regions of involvement is small bowel, colon, esophagus, and rectum respectively (2, 8, 9). Although all subcategories of NHL could be seen, mucosa associated lymphatic tissue and diffuse large B cell subtypes are most seen (1). In some cases multiple involvement of gastrointestinal system could be observed (10).

The percentage of gastrointestinal system differs from patient's age, and race. As such; in some Middle

East countries and Africa small intestine could be the most seen involvement, and in children small intestine is the most involved organ in gastrointestinal system (4). On the other hand the incidence of primary gastrointestinal lymphomas are more frequently observed in Eastern populations than Western populations (4). Even in the same country involvement sites might demonstrate differences. As such, although Dincol et al reported the most common extra-nodal involvement as small intestine (11), data from central and Southern Anatolia, demonstrated that the most common extra-nodal manifestation of NHL is stomach involvement (12, 13).

Primary gastrointestinal system lymphomas are extremely rare, though treatment modalities are controversial, and based on retrospective studies with small sample size. Ann-Arbor, Musshoff, Lugano, Paris TNM grading systems are the most useful grading systems in daily clinical practice.

The aims of this study were 1) To evaluate socio-demographic and disease related factors of NHL patients with stomach involvement, 2) To evaluate

the treatment options, and 3) To demonstrate the differences between South-east coast and Trace region of Turkey.

Materials and Methods

We evaluated NHL patients with primary or secondary stomach involvement between 01/01/1998 and 01/06/2013 retrospectively. In this time period 26 NHL patients with stomach involvement was observed. All pathological samples were obtained by endoscopic punch biopsy or surgical biopsy. All biopsies were evaluated by an experienced hematopathologist at Trakya University Faculty of Medicine, Department of Pathology. Routine H&E staining and Immunohistochemical studies (staining against CD3, CD20, CD5, CD10, CD23, CD30, CD56, and in certain situations Cyclin D1, Bcl -2, Bcl -6, c-myc, p53, Ki-67) were performed. All the patients were classified with WHO classification of tumors of hematopoietic and lymphoid tissues 2008. Cervical, thorax, and abdominal tomography, and/or position emission tomography was used staging the disease. Ann-Arbor (14) and Lugano staging systems (15) were used to evaluate the stage of the disease. Dawson criteria were used to discriminate primary and secondary involvement of gastrointestinal tract (16).

Statistical analysis performed by SPSS version 17. Kolmogorov Smirnov test was used to evaluate normality. Student t test was used to evaluate the differences in medians of continues groups, and Kaplan Meier survival curves were drawn to evaluate the survival rates of different groups. Statistical significance for p value was 0.05.

Results

Mean age at presentation was 60.3 ± 14.8 (32-83). 3 of the patients (11.5%) was female, 23 of the patients (88.5%) was male. 20 of the patients (76.9%) were composed of primary stomach non-Hodgkin lymphoma, 6 of the patients (23.1%) were composed of patients secondary involvement of the advanced stage disease. Mean follow up time was 26.2 ± 34.5 months (1-121 months). 9 (34.6%) patients died during follow up, 13 patients (50%) were still at follow up, and 4 patients (15.4%) were out of follow.

All of the patients were subtypes of B cell lymphoma. Disease was indolent in 3 patients (11.5%), aggressive in 22 patients (84.6%), and very aggressive in 1 of them (3.8%). Diffuse large B cell lymphoma was 72.9%; Maltoma was 8.7%, and Mantle cell lymphoma was 3.8%.

Symptomatic disease was observed in 21 (91.3%) of the patients. Constitutional symptoms was at a ratio of 34.8%. 23.1% of the patients had lymph node hypertrophy. At the time of presentation 6 patients (26.1%) had splenomegaly, 4 patients (17.4%) had hepatomegaly, 6 patients (26.1%) had Bulky disease, and 3 patients (13%) had bone marrow involvement.

24 patients (92.3%) were treated with chemotherapy, 1 patient died because of pulmonary embolism before planned chemotherapy, and 1 patient was treated with antibiotics against early stage Maltoma (3.8%). R-CHOP treatment was the most frequently used chemotherapy regiment at 11 patients (42.3). 5 patients received 2 (23.8%) course, 5 patients received 4 (23.8%) course, 5 patients received 6 (23.8%) course, 6 patients received 8 (%28.6) course of therapy.

Complete response was achieved at 10 patients (55.8%), partial response was achieved in 1 patient (5.6%), and 7 patients were failed to response to treatment. Treatment response of low grade and high grade patients were the same, and overall survival of low grade and high grade patients, both with Ann-Arbor and Lugano classification systems were similar (Figure 1-2). Recurrence was achieved in 4 patients. MINE, (R)-ICE and RFCM treatments were used, and all of the patients who had Recurrence failed the second line treatment and died. Autologous bone marrow treatment could not be able treat patients. Surgical treatment was used in the treatment of 4 of the patients (22.2%). Febrile neutropenia was observed in 4 of the patients (15.4%), 1 patient experienced Kaposi sarcoma (3.8%), and 1 patient (3.8%) experienced pulmonary thromboembolism.

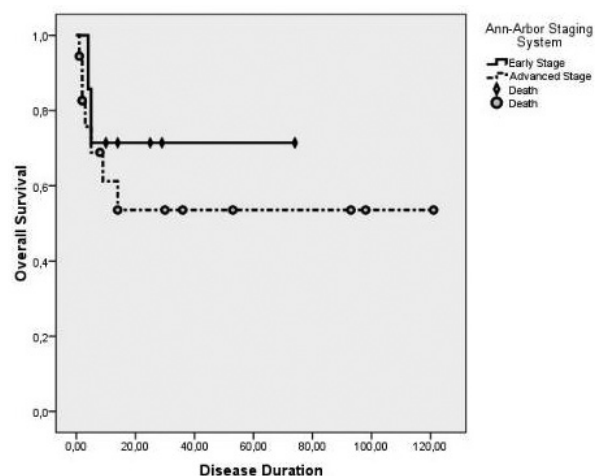


Figure 1. Overall survival difference between early and advanced stage disease according to Ann-Arbor staging system.

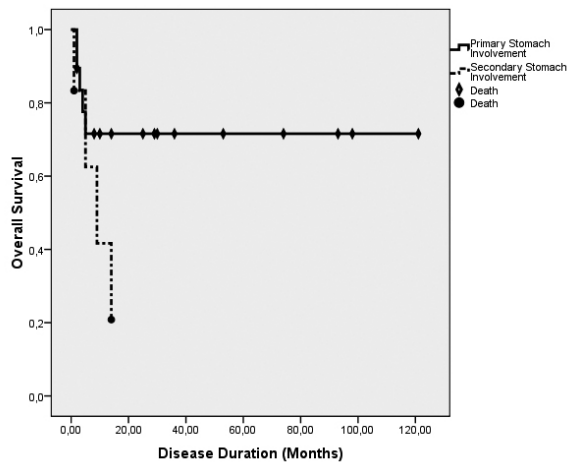


Figure 2. Overall survival difference between early and advanced stage disease according to Lugano staging system.

Mean disease duration was 69.2 ± 12.9 months. In patients with primary stomach involvement overall survival was 87.5 ± 12.7 months. Overall survival in patients with secondary stomach involvement was 8.9 ± 2.4 months. There was no overall survival difference between primary or secondary stomach involvement ($p=0.087$) (Figure 3). There was no difference between low grade and high grade patients due to Ann-arbor staging system were similar due to death.

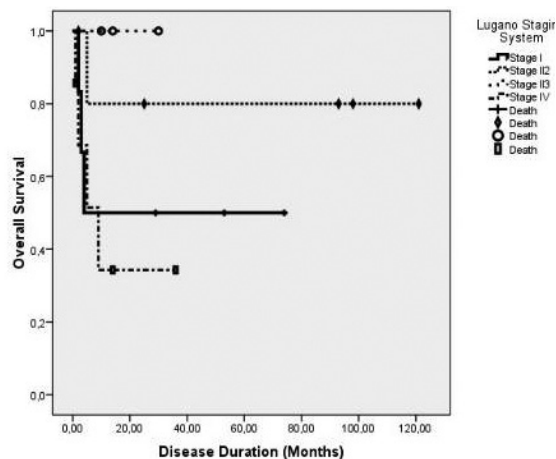


Figure 3. Overall survival difference between primary and secondary stomach involvement.

Sedimentation rate at administration was evaluated for prognosis, and it was found that patients with low sedimentation rate has 88.1 ± 9.3 months of overall survival. Patients with high sedimentation rate has 49.5 ± 19.9 months of overall survival. There was statistically significant difference in overall survival between patients with low and high sedimentation rates ($p=0.027$) (Figure 4). Treatment responses to different chemotherapies were similar.

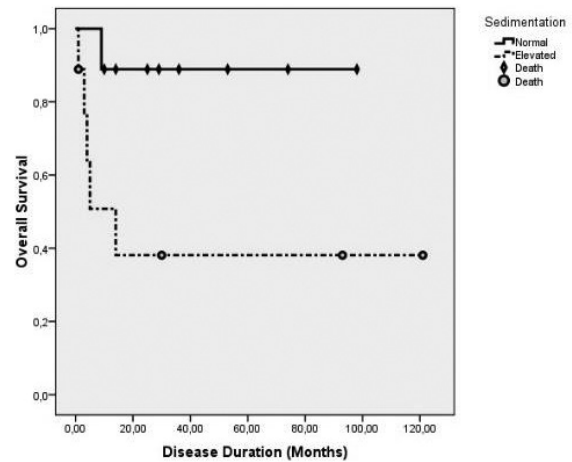


Figure 4. Overall survival difference between elevated or normal sedimentation rate at initial presentation.

Discussion

The most important outcome of our study was observation of similar treatment response and similar overall survival of early stage and advanced stage patients, both with Ann-Arbor and Lugano classification systems. Dincol D. et al had demonstrated that surgery with systematic chemotherapy was superior to chemotherapy alone in early stage primary gastrointestinal lymphoma (11). Whereas in the present study there was no survival difference between early and advanced stage NHL with stomach involvement, so we think that treatment should not be based on disease stage solely. We demonstrated significant lower overall survival rate in patients with higher sedimentation rate, so patients with higher sedimentation rate might be treated with more aggressive treatment options such as more aggressive chemotherapy regimens.

Our study demonstrated similar overall survival in patients treated with or without surgery. We could not demonstrate survival difference in patients treated with chemotherapy with/without surgery in early stage, because of insufficient patient number. So together with recent studies, aggressive treatment without organ preservation should not be performed on patients without higher inflammatory response and early stage presentation (11, 17).

Beyond its retrospective design limitations of our study are composed of small sample size, inclusion of secondary stomach involvement, unable to perform endoscopic sonography, and lack of treatment randomization.

Although studies about extra-nodal gastro-intestinal lymphoma from east, west, southern and central Turkey was published there was a lack of knowledge from Trace region of Turkey. Our study could be evaluated as the missing link in the chain. Because Trace region of Turkey was formed by migration

from Eastern Europe, our study offers the reader to compare socio-demographic and disease related specialties of gastro-intestinal extra-nodal non-Hodgkin's lymphoma within eastern and western populations.

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